

CLAIMS

What is claimed is:

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1. An isolated anti-angiogenic peptide, wherein the C-terminus of the isolated peptide comprises the amino acid sequence SYIVLCIE.
 - 5 2. Isolated EM 1, comprising a mutated endostatin protein, wherein the mutation comprises a deletion of nine consecutive amino acids from the C-terminus of the endostatin protein, and wherein the isolated EM 1 is characterized as having anti-angiogenic activity.
 - 10 3. The isolated EM1 of Claim 2, wherein the C-terminus of the isolated EM 1 comprises the amino acid sequence SYIVLCIE.
 4. The isolated EM 1 of Claim 2, wherein the deletion of nine consecutive amino acids comprises the amino acid sequence NSFMTSFSK.
 - 15 5. The isolated polynucleotide of Claim 1, comprising;
 - (a) the nucleotide sequence of SEQ ID NO:1;
 - (b) a sequence complementary to the nucleotide sequence of SEQ ID NO:1; and
 - (c) a sequence that hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO:1.
 - 20 6. An isolated polynucleotide, comprising the nucleotide sequence amplified by the primers of SEQ ID NO:8 and SEQ ID NO:9.
 7. An isolated polynucleotide of Claim 3, wherein the polynucleotide is operably linked to an expression control sequence.

8. A host cell transformed with the polynucleotide of Claim 7.
9. The host cell of Claim 8, where the cell is selected from the group comprising bacterial, yeast, mammalian, insect or plant cells.
10. A process for producing a protein encoded by the polynucleotide of Claim 5,
5 wherein the process comprises:
 - (a) growing a culture of a host cell transformed with the polynucleotide of Claim 5, where the host cell is selected from the group comprising bacterial, yeast, mammalian, insect or plant cells; and
 - (b) purifying the protein from the culture;10 thereby producing the protein encoded by the polynucleotide of Claim 5.
11. A fusion protein, comprising two or more protein molecules, and further comprising the EM 1 of Claim 3.
12. The fusion protein of Claim 11, further comprising at least one protein molecule selected from the group comprising: restin, endostatin, angiostatin, apomigren, or EM 1.
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13. A composition comprising, as a biologically active ingredient, the EM 1 of Claim 3.
14. The composition of Claim 13, and a pharmaceutically-compatible carrier.
15. A composition comprising, as a biologically active ingredient, the fusion protein
20 of Claim 11.
16. A composition comprising, as a biologically active ingredient, the fusion protein of Claim 12.

17. A method for inhibiting angiogenic activity in mammalian tissue, the method comprising contacting the tissue with a composition comprising the EM 1 of Claim 3.
18. A method of using the composition of Claim 17 to treat a disease, the method comprising administration of the composition to a patient with a disease characterized by angiogenic activity.
19. The method of Claim 18, wherein the disease is selected from the group comprising angiogenesis-dependent cancers, benign tumors, rheumatoid arthritis, psoriasis, ocular angiogenesis diseases, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, wound granulation, intestinal adhesions, atherosclerosis, scleroderma, hypertrophic scars, cat scratch disease, *Helicobacter pylori* ulcers, dialysis graft vascular access stenosis, contraception, and obesity.
20. The method of Claim 19, wherein the disease is cancer.
- 15 21. The method of Claim 20, wherein the disease is renal cancer.
22. A method of using a composition comprising the isolated EM 1 of Claim 3 to induce apoptosis in a cell or tissue, comprising contacting the cell or tissue with the composition.
23. A method of using any of the compositions of Claims 13 to 16 to treat a disease, the method comprising administration of the composition to a patient with a disease characterized by angiogenic activity.
24. The method of Claim 23, wherein the disease is cancer.
25. The method of Claim 24, wherein the disease is renal cancer.

26. A process for providing a mammal with EM 1 protein, the process comprising introducing mammalian cells into a human, said mammalian cells having been treated *in vitro* to insert therein the polynucleotide encoding the amino acid sequence comprising EM 1 and expressing *in vivo* in said mammal a therapeutically effective amount of the EM 1 protein.
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27. The process of Claim 26, wherein the cells are lymphocytes.
28. The process of Claim 27, wherein the lymphocytes are chosen from the group comprising T-lymphocytes and B-lymphocytes.
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29. The process of Claim 26, wherein the cells are chosen from the group comprising: blood cells, TIL cells, bone marrow cells, vascular cells, tumor cells, liver cells, muscle cells, fibroblast cells.
30. The process of Claim 26, wherein the polynucleotide is inserted into the cells by a viral vector.
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31. A process for producing an isolated polynucleotide, the process comprising the steps of:
- (a) preparing one or more polynucleotide probes that hybridize under conditions of moderate stringency to a nucleotide sequence selected from the group consisting of:
- (i) SEQ ID NO:1, from nucleotide 1 to nucleotide 525;
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- (ii) an isolated polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2, from amino acid 1 to amino acid 175; and
- (b) hybridizing said probe(s) to mammalian DNA; and
- (c) isolating the DNA polynucleotide detected with the probe(s);
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- wherein the nucleotide sequence of the isolated polynucleotide corresponds to the nucleotide sequence of SEQ ID NO:1, from nucleotide 1 to nucleotide 525.

32. An isolated polynucleotide produced according to the process of Claim 31.
 33. An isolated polynucleotide comprising the polynucleotide of Claim 32. ✓
 34. Antibodies to the isolated anti-angiogenic mutant fragment of endostatin of Claim 2.
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35. An isolated mutant, derivative, analog or homolog of the EM 1 of Claim 2.